ORIGINAL ARTICLE

Prevalence of Arteriosclerosis and Atherosclerosis in Stable Patients at a Cardiovascular Outpatient Clinic: Potential for Better Care

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Background: Cardiovascular treatment guidelines for stable patients who are regularly followed up at medical center clinics have long been practiced and are intended to improve arteriosclerosis and atherosclerosis in these patients. The present study investigated the prevalence of arteriosclerosis and atherosclerosis in patients attending one such clinic, and explored the potential for better care.

Methods: A total of 124 outpatients randomly selected from 586 stable outpatients on regular visits to the same senior cardiologist were invited to receive measurements of brachial-ankle pulse wave velocity (baPWV) and ankle-brachial index (ABI) using a novel device during their clinic visits. Abnormally high baPWV was defined using the age- and sex-stratified reference ranges obtained from a previous community survey.

Results: The prevalence of high baPWV in the studied outpatients was 24.2% and the prevalence of low ABI (< 0.9) was 8.1%. Based on the reports of baPWV and ABI at the point of care, medications were adjusted in 56 patients (45.2%). In 22 patients who had adjusted antihypertensive medication and repeat examinations of baPWV and ABI at subsequent visits, systolic blood pressure fell by 11 mmHg (p = 0.012), and baPWV fell by 0.2 m/s (p = 0.001).

Conclusion: Abnormal baPWV and ABI are not uncommon in stable patients who are regularly followed up at a cardiology clinic where treatment guidelines are completely followed. Fast assessment of arteriosclerosis and atherosclerosis at the point of care may provide better care for this group of patients. [*J Chin Med Assoc* 2006;69(1):14–20]

Key Words: ankle-brachial index, arteriosclerosis, atherosclerosis, pulse wave velocity

Introduction

Guidelines for the management of cardiovascular risk factors[1–3] and diseases[4,5] have been well established, based on massive series of randomized control trials that showed significant impact on cardiovascular outcomes. Therefore, it is generally agreed that the major barrier to effective cardiovascular prevention is not the lack of evidence but the lack of motivation to follow the guidelines.[6–8] It remains true that strict performance of the guidelines may improve the outcomes of stable patients with cardiovascular risk factors and/or diseases.[7]

Arteriosclerosis,[9] or arterial stiffening,[10] and atherosclerosis[11] are the 2 major underlying pathophysiologies of arterial disease and the primary cause of cardiovascular disease. Both arteriosclerosis[9] and atherosclerosis[11] are markers for future cardiovascular events and are also targets for preventive intervention.[12,13] Pulse wave velocity (PWV) along an arterial segment has been used to assess the extent of arterial stiffening for decades.[14] Ankle-brachial index (ABI), a simple ratio of the systolic blood pressure over the ankle and arm, is a well-recognized index reflecting the extent of atherosclerosis in the coronary and noncoronary arterial beds.[15] It appears reasonable to

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speculate that strict adherence to cardiovascular treatment guidelines for stable patients being long-term followed up would improve arteriosclerosis and atherosclerosis to an extent comparable with that in the low-risk population. Therefore, the present study investigated the prevalence of arteriosclerosis and atherosclerosis in stable patients and explored the potential for better care.

Methods

Study population

A senior cardiologist (C.H.C.) at the Taipei Veterans General Hospital regularly cared for about 60 patients during an outpatient clinic service 3 times a week, prior to the beginning of the study. Among these outpatients, about 10 were new patients on their first visit and 50 were stable patients who had documented chronic cardiovascular diseases and were receiving regular long-term (> 1 year) care at the outpatient clinic. Therefore, the stable patients had paid in total about 600 (50 × 3 × 4 weeks) visits to the same cardiologist. Standard guidelines at the clinic were directed towards the treatment of: hypertension,[1] high blood cholesterol,[3] diabetes mellitus,[16] and chronic heart failure.[17] The study was conducted in 12 consecutive cardiology clinic services in 4 weeks. During each study clinic service, 1 of every 5 patients, according to the actual order of entering the clinic office, was offered a free examination of baPWV and ABI, if he or she was not a new patient. The selected patients were guided to another room nearby for examination and returned to the clinic office about 20 minutes later with the report for interpretation and further management. About 10 patients were selected in a clinic service session and, in total, 124 patients were selected from a total of 586 stable patients in the 12 study clinic services. Medical diagnosis, personal history, and prescription of cardiovascular medications were recorded in a case report form for all 586 stable patients.

Assessment of arteriosclerosis and atherosclerosis

The measurements of baPWV and ABI were performed using a novel device (VP-1000; Colin Corporation, Komaki, Japan) with well-documented validity and reproducibility.[18] Personal data, including identification number, date of birth, height, and weight were entered through the front panel of the device while participants were resting in the supine position. Pneumatic pressure cuffs were placed snugly around both arms and both ankles. Electrocardiographic electrodes were attached on both wrists, and a microphone for phonocardiography was placed at the second intercostal space at the left margin of the sternum. After completion of the preparation, the fully automatic data acquisition and processing procedure started with the simultaneous measurements of blood pressure over the 4 extremities by the oscillometric principle, followed by pulse volume recording over the right arm and both ankles for 10 seconds when the cuff pressures were maintained at a level of 60 mmHg. The recorded cuff pressure signals during pulse volume recording are known as the pulse volume traces and have been found to correspond to the intra-arterial pressure contours.[19] The simultaneously recorded pulse volume traces were processed instantaneously to provide the pulse transit time (foot-to-foot intervals) between right arm and right ankle, and between left arm and left ankle, respectively. Physiologically, the pulse travels from the heart to the arms and ankles, separately, in opposite directions, and not in a direction from the arm to the ankle. Therefore, the time difference between the arm and ankle pulse volume traces was assumed to correspond to the different transit times required for the pulse to travel from the heart to the arm and ankle, respectively. The corresponding distance for the time difference was, therefore, calculated as the difference between the heart-to-ankle and heart-to-arm distances, and was automatically estimated from height according to the following regression equation: distance = 0.5934 × height + 14.401. Thereafter, the right brachial-to-right ankle pulse wave velocity (rbaPWV) was calculated automatically as the distance divided by the transit time between the right arm and right ankle, and left brachial-to-left ankle pulse wave velocity (lbaPWV) as the distance divided by transit time between the left arm and left ankle. The right ankle-brachial index (rABI) was directly calculated as the right ankle systolic blood pressure divided by the higher brachial systolic blood pressure, and the left ankle-brachial index (lABI) was calculated as the left ankle systolic blood pressure divided by the higher brachial systolic blood pressure. Complete measurements of all pulse wave velocities and ABIs were usually finished in less than 5 minutes.

Data analysis

In the present study, supine right-arm systolic and diastolic blood pressures measured using the VP-1000 were used for all analyses. Because a long pulse transit time is anticipated with resultant lower PWV in the presence of peripheral arterial disease in the lower extremities, we, therefore, selected the higher between rbaPWV and lbaPWV as the representative baPWV for indexing arteriosclerosis. Similarly, we selected the lower between rABI and lABI as the representative ABI for indexing atherosclerosis.

The age- and sex-stratified normal reference values (means and standard deviations) of the baPWV were derived from a previous community survey performed in Kinmen.[20] High baPWV was defined as a value higher than the upper limit of the normal reference (mean plus 2 standard deviations). An ABI < 0.9 was considered to indicate peripheral arterial disease and the presence of systemic atherosclerosis.[21]

Clinical decision making

Because the participants as stable patients had been followed up at the clinic for a long time, most of the hypertensive patients had attained reasonably good blood pressure control. Therefore, a high blood pressure at clinic was usually not sufficient to up-titrate the current antihypertensive medication unless it was confirmed subsequently by a good record of 1-month home blood-pressure monitoring or a 24-hour ambulatory blood-pressure monitoring. With the availability of baPWV and ABI at the point of care, the cardiologist was able to make immediate decisions for the study patients. Since high PWV in a hypertensive patient might indicate inappropriate antihypertensive treatment, the cardiologist, therefore, subjectively decided to adjust the antihypertensive agents accordingly to up-titrate the dosage or add another antihypertensive medication if the baPWV was obviously beyond the normal reference range. Different classes of antihypertensive agents were chosen based on the hypertension treatment guidelines[1] because it is, so far, generally accepted that diuretics, calcium channel blockers, and angiotensin-converting enzyme inhibitors share a similar ability to decrease arterial stiffness in hypertensive patients.[22]

The antihypertensive dosage would also be down-titrated if the systolic blood pressure at clinic was too low and the baPWV was obviously within the normal range.

In a patient with occult peripheral arterial disease defined by ABI < 0.9 but without symptoms, the cardiologist would decide to intensify medical treatment according to the treatment guidelines.[23]

Statistical analysis

Results are expressed as mean ± SD. Between-group comparisons were performed using the paired *t*-test or Chi-square test where appropriate. Within-group comparisons were performed using the paired Student *t*-test. Statistical significance was set at the $p < 0.05$ level. Multivariate logistic regression analysis was performed to determine the predictors of high baPWV and/or low ABI.

Results

Characteristics of the study population

A total of 124 patients were randomly selected for rapid assessment of arteriosclerosis and atherosclerosis from 586 stable patients in 12 study clinic services. The selected and unselected patients were similar except that the prescription of sulfonylurea was significantly less common in the selected patients (4.9% vs 11.4%, $p < 0.05$) (Table 1). The selected patients were 83 men and 41 women with a mean age of 67.4 years (range, 26–90 years). The most frequent cardiovascular diagnosis was hypertension (70.7%), followed by ischemic heart disease (56.9%).

Prevalence of high baPWV

Table 2 summarizes the anthropometric and hemodynamic measurements provided by the VP-1000 in 124 stable outpatients at the cardiology clinic. Figure 1A displays the age- and sex-stratified prevalence of high baPWV against the reference values obtained from the previous community survey in Kinmen. Overall, 24.2% of patients (16.9% of men and 39.0% of women) under regular treatment had high baPWV.

Prevalence of low ABI

The age- and sex-stratified prevalence of low ABI (ABI < 0.9) is shown in Figure 1B. The overall prevalence of low ABI was 8.1% (7.2% in men and 9.8% in women). The prevalence of low ABI was very low until the age of 70 years. Among the 9 patients with low ABI, only 1 had symptoms of peripheral arterial disease. The prevalence of occult peripheral arterial disease was, therefore, 6.5%.

Characteristics of patients with high baPWV and/or low ABI

Table 3 shows the comparison between patients with high baPWV and/or low ABI and those with normal baPWV and ABI. Patients with high baPWV and/or low ABI were characterized by dominance of women, lower prevalence of smoking, higher prevalence of renal function impairment, and higher systolic blood pressure. The independent predictors of high baPWV and/or low ABI identified by multivariate logistic regression analysis included female sex (odds ratio 7.69, 95% confidence interval 1.23–47.6, $p = 0.029$), systolic blood pressure (odds ratio 1.07, 95% CI 1.03–1.11, $p = 0.001$), and diabetes (odds ratio 3.91, 95% confidence interval 0.98–15.72, $p = 0.054$). Age, body mass index, triglycerides, high-density lipoprotein cholesterol, and smoking status were not significant predictors.

Table 1. Characteristics among selected, unselected, and all outpatients

	Selected (n = 124)	Unselected (n = 462)	All (n = 586)
Age, yr (± SD)	67.4 ± 13.1	67.7 ± 13.9	67.7 ± 13.7
Sex, % male	66.7	59.6	61.1
Smoking, %	53.7	49.2	50.2
Hypertension, %	70.7	73.4	72.9
Ischemic heart disease, %	56.9	54.4	55.0
Valvular heart disease, %	16.3	19.2	18.6
Congenital heart disease, %	0.81	0.43	0.51
Stroke, %	1.63	3.02	2.73
Peripheral arterial disease, %	0.81	2.80	2.39
Carotid artery disease, %	4.07	6.05	5.63
Diabetes mellitus, %	20.3	23.97	23.21
Dyslipidemia, %	45.5	47.08	46.76
Atrial fibrillation, %	6.50	7.13	7.00
PTCA, %	4.87	5.83	5.63
CABG, %	4.07	5.18	4.94
Renal function impairment, %	7.3	5.4	5.8
Congestive heart failure, %	9.8	9.9	9.9
Angiotensin-converting enzyme inhibitors, %	36.6	35.9	36.0
Angiotensin II blockers, %	30.1	26.4	27.1
Calcium channel blockers, %	51.2	53.1	52.7
Diuretics, %	43.1	46.4	45.7
Antiplatelet agent, %	52.0	55.5	54.8
α-blocker, %	11.4	8.9	9.4
β-blocker, %	37.4	38.7	38.4
Statins, %	19.5	21.2	20.8
Fibrate, %	1.6	4.1	3.6
Sulfonylurea, %	4.9	11.4*	10.1
Biguanide, %	4.9	7.6	7.0
AGI, %	0	1.08	0.85
Insulin sensitizer, %	4.9	2.6	3.1
Insulin, %	0.8	1.0	1.0

$p < 0.05$ as compared with the selected group. AGI = α-glucosidase inhibitor; CABG = coronary artery bypass graft; PTCA = percutaneous transluminal coronary angiography.

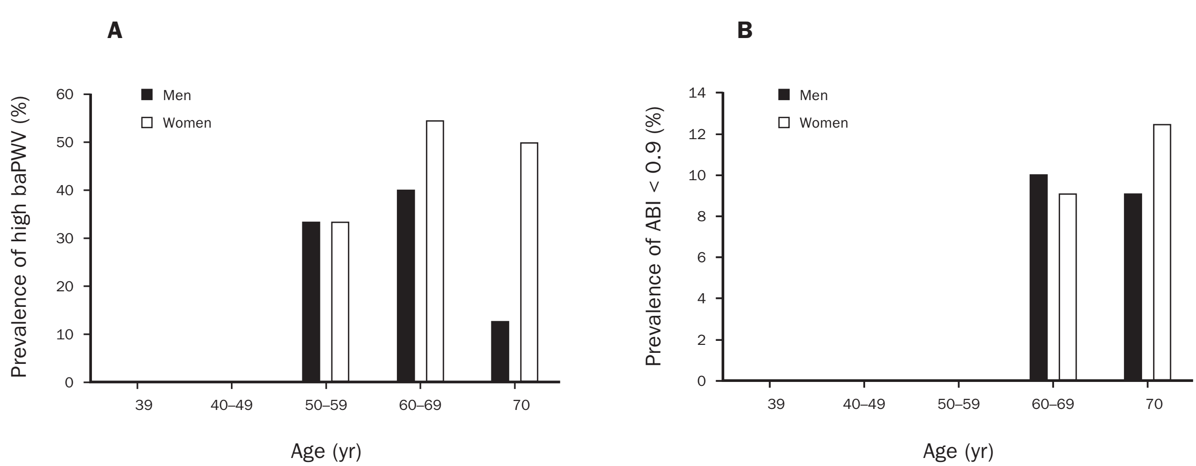

Figure 1. Age- and sex-stratified prevalence of high baPWV (A) and ABI < 0.9 (B) in the 124 stable cardiology outpatients.

Table 2. Summary of the anthropometric and hemodynamic parameters in the selected 124 stable cardiology outpatients

Variables	Mean ± SD	Range
Height, cm	162.9 ± 7.9	147–187
Weight, kg	63.3 ± 11.8	26–90
Waist, cm	84.6 ± 9.7	52–111
Heart rate, beats/min	68.3 ± 10.9	38–94
Right-arm SBP, mmHg	132.6 ± 18.8	78–190
Right-arm DBP, mmHg	74.5 ± 11.3	44–103
Left-arm SBP, mmHg	130.5 ± 19.2	74–179
Left-arm DBP, mmHg	73.9 ± 10.5	47–101
Right-ankle SBP, mmHg	146.5 ± 28.3	47–232
Right-ankle DBP, mmHg	73.3 ± 12.2	22–102
Left-ankle SBP, mmHg	144.2 ± 28.8	62–217
Left-ankle DBP, mmHg	72.0 ± 12.0	27–103
rABI	1.08 ± 0.10	0.60–1.32
lABI	1.07 ± 0.11	0.53–1.30
rbaPWV, m/s	1.8 ± 0.5	1.1–4.2
lbaPWV, m/s	1.8 ± 0.5	1.1–4.2

DBP = diastolic blood pressure; lABI = left ankle-brachial index; lbaPWV = left brachial-ankle pulse wave velocity; rABI = right ankle-brachial index; rbaPWV = right brachial-ankle pulse wave velocity; SBP = systolic blood pressure.

Table 3. Comparison of patients with and without high baPWV and/or low ABI

	High baPWV and/or low ABI (n = 41)	Normal baPWV and ABI (n = 83)	p value
Age, yr (± SD)	70.3 ± 12.5	65.6 ± 13.7	0.069
Age ≥ 65 yr, %	70.7	62.7	0.374
Male, %	48.8	75.9	0.003
Total cholesterol, mg/dL (± SD)	146.9 ± 100.7	154.4 ± 91.3	0.676
Triglycerides, mg/dL (± SD)	101.6 ± 88.8	104.2 ± 97.2	0.887
HDL cholesterol, mg/dL (± SD)	32.8 ± 29.8	31.8 ± 27.2	0.860
LDL cholesterol, mg/dL (± SD)	135.2 ± 41.4	133.3 ± 40.9	0.836
LDL cholesterol >130 mg/dL, %	44.8	53.2	0.455
HDL cholesterol < 40 mg/dL, %	53.7	45.8	0.409
SBP, mmHg (± SD)	139.3 ± 22.5	127.7 ± 15.3	0.004
Hypertension, %	65.9	73.5	0.378
Diabetes, %	26.8	16.9	0.193
BMI ≥ 25 kg/m^2, %	23.3	38.2	0.150
Smoking, %	39.0	60.2	0.026
Renal function impairment, %	19.5	1.2	0.001
Angiotensin-converting enzyme inhibitors, %	39.0	36.1	0.755
Calcium channel blocker, %	58.5	48.2	0.278
Diuretics, %	51.2	38.6	0.180
Antiplatelet agent, %	48.8	54.2	0.569
α-blocker, %	14.6	9.6	0.408
β-blocker, %	29.3	41.0	0.205
Statins, %	19.5	19.3	0.975
Fibrate, %	2.4	1.2	0.608
Sulfonylurea, %	7.3	3.6	0.366
Biguanide, %	9.8	2.4	0.073
AGI, %	0.0	0.0	—
Insulin, %	2.4	0.0	0.153
Insulin sensitizer, %	2.4	6.0	0.381

ABI = ankle-brachial index; AGI = α-glucosidase inhibitor; BMI = body mass index; baPWV = brachial-ankle pulse wave velocity; HDL = high-density lipoprotein; LDL = low-density lipoprotein; SBP = systolic blood pressure.

New clinical decisions

Based on the readily available reports of baPWV and ABI at the clinic, the cardiologist judged to adjust the medications in 56 patients (45.2%). In brief, new classes of antihypertensive drugs were added in 33.9%, original drugs up-titrated in 6% and down-titrated in 3% of patients.

As compared with subjects without adjustment of medication, subjects with medication adjusted were older (71.8 ± 10.2 vs 63.4 ± 14.6 years old, $p = 0.0003$) and had higher systolic blood pressure (140 ± 17.6 vs 124.5 ± 16.8 mmHg, $p < 0.0001$) and baPWV (2.11 ± 0.50 vs 1.65 ± 0.36 m/s, $p < 0.0001$).

Follow-up of baPWV and ABI

Of the 124 subjects enrolled for the survey, 47 received repeat examination of baPWV and ABI during subsequent visits. In the 22 patients who had their antihypertensive medication adjusted (all up-titrated), systolic blood pressure fell by 11 mmHg (from 145 ± 13 mmHg at baseline to 134 ± 18 mmHg, $p = 0.012$), baPWV fell by 0.2 m/s (from 2.3 ± 0.6 to 2.0 ± 0.6 m/s, $p = 0.001$), while ABI did not change (from 1.07 ± 0.09 to 1.07 ± 0.09). In the 25 patients who maintained previous antihypertensive medication, no significant changes over systolic blood pressure (from 129 ± 16 to 129 ± 17 mmHg), baPWV (from 1.9 ± 0.4 to 1.8 ± 0.3 m/s), and ABI (from 1.04 ± 0.10 to 1.07 ± 0.10) were observed.

Discussion

The present study demonstrated that, in stable cardiology patients on regular cardiovascular treatment, the percentage of abnormally high baPWV and low ABI may rise up to 24.2% and 8.1%, respectively. This may imply that a substantial proportion of stable patients who are followed up regularly in a cardiology clinic are not receiving optimal treatment. This study further suggests that the availability of rapid assessment of arteriosclerosis and atherosclerosis at the point of care may result in new decision making in a substantial proportion of patients to achieve better care.

In our previous community-based survey in Kinmen, the overall prevalence of high baPWV was 27.1% for men and 25.4% for women.[20] It is interesting to know that the prevalence of high baPWV is similar in stable patients regularly followed up at a cardiology clinic and in residents of a community with limited medical resources. On the other hand, the overall prevalence of low ABI in Kinmen was very low (2.8% for men and 1.7% for women), as compared with that in the present study. It is anticipated that many of the cardiology patients had established cardiovascular disease and significant arteriosclerosis and atherosclerosis. Not surprisingly, they might have higher prevalence of low ABI than community residents. However, it remains to be demonstrated if high PWV can be completely normalized with optimal current cardiovascular therapy.

Although both PWV and ABI can be measured noninvasively and are commonly used in clinical or community research, PWV has hardly been used clinically and ABI is only indicated clinically as part of assessments for patients with suspected peripheral arterial disease. More importantly, measurements of PWV and ABI by separate conventional methods are usually time-consuming and performed at a vascular laboratory distant from the outpatient clinic, and are, therefore, not readily available for clinical decision making during the same clinic visit.

Recently, a novel device (VP-1000) was developed for simultaneous performance of pulse volume recording over both arms and both ankles to automatically generate the baPWV and ABI in less than 5 minutes.[18,24] With this technology, the indexes for both arteriosclerosis and atherosclerosis are now as conveniently available at the point of care (at an outpatient clinic or on a ward) as an electrocardiogram or a chest X-ray film.

Peripheral arterial disease is a progressive condition associated with an elevated risk of heart attack and stroke. Most cases are asymptomatic and the patients face an increased risk of heart attack, stroke, and death, whether or not the disease is symptomatic.[25] The identification of 8.1% asymptomatic patients with peripheral arterial disease in the current study confirms the disease to be a largely undiagnosed and undertreated entity.[25] More aggressive risk factor intervention along with the administration of evidence-based medication[26] is necessary to reduce future cardiovascular risk.[25]

Although there are clear guidelines for the management of patients with peripheral arterial disease,[25,27] it remains empirical to adjust the treatment protocol based on the findings of PWV. The decisions to adjust medications for patients with abnormal baPWV in this study were made solely according to the senior cardiologist's subjective judgment, due to the lack of strict criteria or guidelines.[22] In addition, the impact of the new decisions on the outcomes remains to be determined in future studies.

In conclusion, abnormal baPWV and ABI are not uncommon in stable patients who are followed up regularly at a cardiology clinic. Clinically, fast assessment of arteriosclerosis and atherosclerosis may have a potential for improving the quality of care.

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